```
stn


Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:ssspta1612bxr

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  JUL 28  CA/CAplus patent coverage enhanced
 NEWS  3  JUL 28  EPFULL enhanced with additional legal status
                  information from the epoline Register
 NEWS  4  JUL 28  IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
 NEWS  5  JUL 28  STN Viewer performance improved
 NEWS  6  AUG 01  INPADOCDB and INPAFAMDB coverage enhanced
 NEWS  7  AUG 13  CA/CAplus enhanced with printed Chemical Abstracts
                  page images from 1967-1998
 NEWS  8  AUG 15  CAOLD to be discontinued on December 31, 2008
 NEWS  9  AUG 15  CAplus currency for Korean patents enhanced
 NEWS 10  AUG 27  CAS definition of basic patents expanded to ensure
                  comprehensive access to substance and sequence
                  information
 NEWS 11  SEP 18  Support for STN Express, Versions 6.01 and earlier,
                  to be discontinued
 NEWS 12  SEP 25  CA/CAplus current-awareness alert options enhanced
                  to accommodate supplemental CAS indexing of
                  exemplified prophetic substances
 NEWS 13  SEP 26  WPIDS, WPINDEX, and WPIX coverage of Chinese and
                  and Korean patents enhanced
 NEWS 14  SEP 29  IFICLS enhanced with new super search field
 NEWS 15  SEP 29  EMBASE and EMBAL enhanced with new search and
                  display fields
 NEWS 16  SEP 30  CAS patent coverage enhanced to include exemplified
                  prophetic substances identified in new Japanese-
                  language patents
 NEWS 17  OCT 07  EPFULL enhanced with full implementation of EPC2000
 NEWS 18  OCT 07  Multiple databases enhanced for more flexible patent
                  number searching
 NEWS 19  OCT 22  Current-awareness alert (SDI) setup and editing
                  enhanced
 NEWS 20  OCT 22  WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT
                  Applications
 NEWS 21  OCT 24  CHEMLIST enhanced with intermediate list of
                  pre-registered REACH substances

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.



Updated Search
```

stn

```
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:30:09 ON 26 OCT 2008

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 16:30:25 ON 26 OCT 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   24 OCT 2008  HIGHEST RN 1065816-63-8
DICTIONARY FILE UPDATES:  24 OCT 2008  HIGHEST RN 1065816-63-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Documents and Settings\brobinson1\My Documents\e-Red
Folder\10524345\nji.str

L1      STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 16:39:02 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      773 TO ITERATE
```

Updated Search

stn

100.0% PROCESSED 773 ITERATIONS 4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 13792 TO 17128
PROJECTED ANSWERS: 4 TO 200

L2 4 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 177.90 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:39:07 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 15082 TO ITERATE

100.0% PROCESSED 15082 ITERATIONS 80 ANSWERS
SEARCH TIME: 00.00.02

L3 80 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 184.80 185.01

FILE 'HCAPLUS' ENTERED AT 16:39:11 ON 26 OCT 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 26 Oct 2008 VOL 149 ISS 18
FILE LAST UPDATED: 24 Oct 2008 (20081024/ED)

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the second quarter of 2008.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l3
L4 29 L3

Updated Search

stn

=> s ll and matsuoka, h?/au
          8520 LL
           570 LLS
          9046 LL
                (LL OR LLS)
          2772 MATSUOKA, H?/AU
L5   1 LL AND MATSUOKA, H?/AU

=> d l4, ibib abs hitstr, l

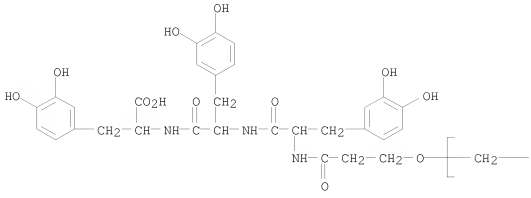
L4   ANSWER 1 OF 29 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:860091 HCAPLUS
DOCUMENT NUMBER: 149:154921
TITLE: Antifouling coatings and their manufacture
INVENTOR(S):   Messersmith, Phillip; Statz, Andrea R.; Lee, Bruce P.;
                          Dalsin, Jeffrey L.; Sherman, Daniel
PATENT ASSIGNEE(S):   USA
SOURCE: U.S. Pat. Appl. Publ., 16pp.
                          CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

     PATENT NO.   KIND   DATE   APPLICATION NO.   DATE
     ---------------   ----   --------   --------------------   --------
     US 20080171012   A1   20080717   US 2008-972008   20080110
     WO 2008089032   A1   20080724   WO 2008-US50721   20080110
         W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
             CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES,
             FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
             KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
             ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
             PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
             IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
             TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:   US 2007-879873P   P 20070111
AB   A method to reduce or eliminate marine biofouling of various surfaces
     comprises treating surfaces with mPEG-DOPA, which is monomethoxy
     polyoxyethylene conjugated with L-3-(3,4-dihydroxyphenyl)alanine. The
     hydrophilic m-PEG-DOPA resulted antifouling ability equivalent to
     polydimethylsiloxane elastomer for Ulva, but better performance for diatom
     Navicula.
IT   833489-84-2
     RL: PRP (Properties); TEM (Technical or engineered material use); USES
     (Uses)
        (methoxy polyoxyethylene conjugated with dihydroxypenylalanine as
        hydrophilic antifouling agents)
RN   833489-84-2 HCAPLUS
CN   Poly(oxy-1,2-ethanediyl), α-methyl-ω-hydroxy-, lN-ether with
     3-hydroxy-N-(3-hydroxy-1-oxopropyl)-L-tyrosyl-3-hydroxy-L-tyrosyl-3-

stn

hydroxy-L-tyrosine (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

```
=> d his

     (FILE 'HOME' ENTERED AT 16:30:09 ON 26 OCT 2008)

     FILE 'REGISTRY' ENTERED AT 16:30:25 ON 26 OCT 2008
L1             STRUCTURE UPLOADED
L2               4 S L1
L3              80 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 16:39:11 ON 26 OCT 2008
L4              29 S L3
L5               1 S LL AND MATSUOKA, H?/AU

=> s l4 not l5
L6              29 L4 NOT L5
```

Updated Search

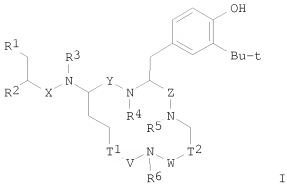
```
stn



=> s l4 not l5
L7          29 L4 NOT L5

=> s l4 and sato, t?/au
         26063 SATO, T?/AU
L8           0 L4 AND SATO, T?/AU

=> s l6 and takahashi, t?/au
         21947 TAKAHASHI, T?/AU
L9           0 L6 AND TAKAHASHI, T?/AU

=> file reg
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                  18.90     203.91

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                     ENTRY    SESSION
CA SUBSCRIBER PRICE                                  -0.80      -0.80

FILE 'REGISTRY' ENTERED AT 16:42:14 ON 26 OCT 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   24 OCT 2008  HIGHEST RN 1065816-63-8
DICTIONARY FILE UPDATES:  24 OCT 2008  HIGHEST RN 1065816-63-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Documents and Settings\brobinson1\My Documents\e-Red
Folder\10524345\asdfaertt.str

L10     STRUCTURE UPLOADED

=> d l10
L10 HAS NO ANSWERS
L10             STR




Updated Search
```

```
stn

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l10
SAMPLE SEARCH INITIATED 16:44:48 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    20094 TO ITERATE

 10.0% PROCESSED     2000 ITERATIONS                                 4 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       393392 TO   410368
PROJECTED ANSWERS:             423 TO     1183

L11           4 SEA SSS SAM L10

=> s l10 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 177.90 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:44:52 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   404547 TO ITERATE

100.0% PROCESSED   404547 ITERATIONS                               414 ANSWERS
SEARCH TIME: 00.00.15

L12         414 SEA SSS FUL L10

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    180.20     384.11

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                      0.00      -0.80

FILE 'HCAPLUS' ENTERED AT 16:45:11 ON 26 OCT 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.
```

Updated Search

```
stn


FILE COVERS 1907 - 26 Oct 2008  VOL 149 ISS 18
FILE LAST UPDATED: 24 Oct 2008  (20081024/ED)

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the second quarter of 2008.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s l12
L13          8 L12

=> s l13 and matsuoka, h?/au
          2772 MATSUOKA, H?/AU
L14          2 L13 AND MATSUOKA, H?/AU

=> d l14, ibib abs fhitstr, 1-2

L14  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2002:157810  HCAPLUS
DOCUMENT NUMBER:          136:217049
TITLE:                    Preparation of cyclic peptide derivatives as motilin
                          receptor antagonists
INVENTOR(S):              Matsuoka, Hiroharu; Sato, Tsutomu
PATENT ASSIGNEE(S):       Chugai Seiyaku Kabushiki Kaisha, Japan
SOURCE:                   PCT Int. Appl., 89 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     --------------      ----   --------    -------------------     --------
     WO 2002016404        A1    20020228    WO 2001-JP7213          20010823
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
            PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
            US, UZ, VN, YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
            DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2001080120        A     20020304    AU 2001-80120           20010823
     EP 1312612           A1    20030521    EP 2001-958426          20010823
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     US 20030191053       A1    20031009    US 2003-362574          20030224
     US 7018981           B2    20060328
PRIORITY APPLN. INFO.:                     JP 2000-253950      A  20000824
                                           WO 2001-JP7213      W  20010823
OTHER SOURCE(S):          MARPAT 136:217049
GI



Updated Search
```

stn



I

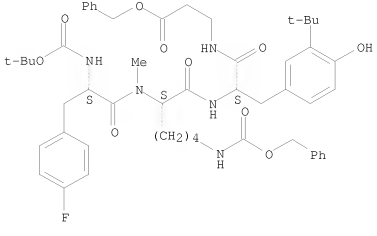
AB The title compds. I [T1 = (CH2)m; T2 = (CH2)n; R1 represents optionally substituted Ph, etc.; R2 represents amino, etc.; R3 to R6 each represents hydrogen, Me, etc.; V, W, X,Y, Z represent carbonyl or methylene; m is an integer of 0 to 2; and n is an integer of 0 to 3] are prepared In an in vitro test for motilin receptor antagonism, (2S-(2S,12S))-2-amino-N-(2-(3-tert-butyl-4-hydroxylphenylmethyl)-1,4,8-triaza-3,7,13-trioxocyclotridecan-12-yl)-3-(4-fluorophenyl)-N-methylpropionamide showed IC50 of 0.52 nM.

IT 401896-13-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cyclic peptide derivs. as motilin receptor antagonists)

RN 401896-13-7 HCAPLUS

CN β-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-4-fluoro-L-phenylalanyl-N2-methyl-N6-[(phenylmethoxy)carbonyl]-L-lysyl-3-(1,1-dimethylethyl)-L-tyrosyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Updated Search

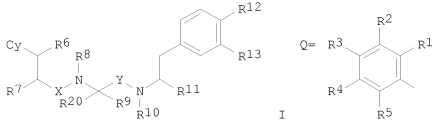
stn

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:535162 HCAPLUS
DOCUMENT NUMBER: 133:150920
TITLE: Preparation of peptides or analogs containing substituted phenethylamine moiety as motilin receptor antagonists
INVENTOR(S): Matsuoka, Hiroharu; Sato, Tsutomu; Takahashi, Tadakatsu; Kim, Dong Ick; Jung, Kyung Yun; Park, Chan Hee
PATENT ASSIGNEE(S): Chugai Seiyaku Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 403 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044770	A1	20000803	WO 2000-JP444	20000128
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2359030	A1	20000803	CA 2000-2359030	20000128
EP 1149843	A1	20011031	EP 2000-901956	20000128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
HU 2001005204	A2	20020429	HU 2001-5204	20000128
HU 2001005204	A3	20020528		
JP 3715202	B2	20051109	JP 2000-596026	20000128
NO 2001003684	A	20010928	NO 2001-3684	20010726
PRIORITY APPLN. INFO.:			JP 1999-20523 A	19990128
			JP 1999-283163 A	19991004
			WO 2000-JP444 W	20000128
OTHER SOURCE(S):	MARPAT 133:150920			

GI



I

Updated Search

stn

AB Substituted phenethylamine derivs. represented by general formula (I), hydrates of the same, or pharmaceutically acceptable salts thereof [wherein Cy is a group represented by general formula Q, an optionally substituted heterocyclic group, C3-7 cycloalkyl, or phenyl; R1, R1, R1, R1 and R5 are each hydrogen, halogeno, hydroxyl, amino, trifluoromethyl or cyano, at least one of R1-R5 being halogeno, trifluoromethyl or cyano; R6 represents hydrogen, (un)substituted linear or branched C1-3 alkyl, amino, or hydroxy; R8 represents hydrogen, Me, or ethyl; R9 represents (un)substituted linear or branched C1-6 alkyl, C2-6 alkenyl, or C2-6 alkynyl, C3-7 cycloalkyl, or (un)substituted Ph; R20 represents hydrogen, or (un)substituted linear or branched C1-3 alkyl or R9 and R20 together forms C3-7 cycloalkyl; R10 represents hydrogen, (un)substituted linear or branched C1-3 alkyl; R11 represents hydrogen or (un)substituted linear or branched C1-3 alkyl, (un)substituted carbamoyl, or carboxy; R12 represents hydroxy or linear or branched C1-4 alkoxy; R13 represents hydrogen, (un)substituted linear or branched C1-6 alkyl, C2-6 alkenyl, or alkynyl, etc.; X, Y represents carbonyl or CH2; provisos are given.], which exhibit motilin receptor antagonism and being useful as drugs for preventing digestive tract movement or high level of blood motilin. Thus, 3-methyl-2-methylaminobutyric acid 2-(3-tert-butyl-4-hydroxyphenyl)-1-(2-pyridylcarbamoyl)ethylamide (preparation given) was condensed with Boc-Phe(4-F)-OH using CMPI in the presence of Et3N in THF under ice-cooling for 4 h followed by treatment of the product with CF3CO2H in CH2Cl2 gave 2-((2-amino-3-(4-fluorophenyl)propanoyl)-N-methylamino)-3-methylbutyric acid 2-(3-tert-butyl-4-hydroxyphenyl)-1-(2-pyridylcarbamoyl)ethylamide (II). II and N-Et-Phe(4-F)-N-Me-Val-N-Et-Tyr(3-tBu)-NHEt showed IC50 of 0.35 and 0.17 nM, resp., for inhibiting binding of 125I-motilin to motilin receptor preparation from mucous membrane of rabbit duodenum.

IT 287205-81-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides or analogs containing substituted phenethylamine moiety
as motilin receptor antagonists and drugs for preventing digestive tract movement or high level of blood motilin)

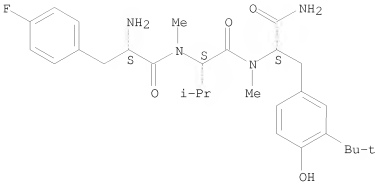
RN 287205-81-6 HCAPLUS

CN L-Tyrosinamide, 4-fluoro-L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)-Nα-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Updated Search

stn



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> d his

     (FILE 'HOME' ENTERED AT 16:30:09 ON 26 OCT 2008)

     FILE 'REGISTRY' ENTERED AT 16:30:25 ON 26 OCT 2008
L1               STRUCTURE UPLOADED
L2             4 S L1
L3            80 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 16:39:11 ON 26 OCT 2008
L4            29 S L3
L5             1 S LL AND MATSUOKA, H?/AU
L6            29 S L4 NOT L5
L7            29 S L4 NOT L5
L8             0 S L4 AND SATO, T?/AU
L9             0 S L6 AND TAKAHASHI, T?/AU

     FILE 'REGISTRY' ENTERED AT 16:42:14 ON 26 OCT 2008
L10              STRUCTURE UPLOADED
L11            4 S L10
L12          414 S L10 FULL

     FILE 'HCAPLUS' ENTERED AT 16:45:11 ON 26 OCT 2008
L13            8 S L12
L14            2 S L13 AND MATSUOKA, H?/AU

=> s l13 not l14
L15            6 L13 NOT L14

=> s l15 and sato, t?/au
         26063 SATO, T?/AU
L16            2 L15 AND SATO, T?/AU

=> d l16, ibib abs hitstr, 1-2

L16  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2002:90066  HCAPLUS
```

Updated Search

stn

DOCUMENT NUMBER: 136:135034
TITLE: Method for producing tripeptide derivative
INVENTOR(S): Sato, Tsutomu; Shimizu, Hirohito
PATENT ASSIGNEE(S): Chugai Seiyaku Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008248	A1	20020131	WO 2001-JP6295	20010719
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2005097119	A	20050414	JP 2000-219977	20000721
PRIORITY APPLN. INFO.:			JP 2000-219977 A	20000721

OTHER SOURCE(S): CASREACT 136:135034; MARPAT 136:135034
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

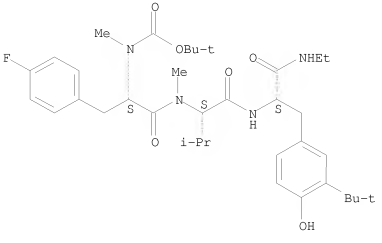
AB A method for producing L-phenylalanyl-L-valyl-L-3-tert-butyl-L-tyrosinamide compds. represented by the general formula (I; wherein R1 represents a hydrogen atom or a linear or branched aliphatic alkyl group having 1 to 4 carbon atoms; R2 represents a hydrogen atom or Me group; R3 represents a hydrogen atom or Me group; and R4 represents a halogen atom) comprises condensation of 3-tert-butyl-L-tyrosinamide derivs. (II; R1 , R2 = same as above) with N-methyl-L-valine derivs. (III; P1 = amino-protecting group), N-deprotection of the resulting L-valyl-3-tert-butyl-L-tyrosinamide derivs. (IV; R1, R2, P1 = same as above), and condensation of the resulting IV (P1 = H; R1 , R2 = same as above) with L-phenylalanine derivs. (V; R3, R4 = same as above; P2 = amino-protecting group) followed by N-deprotection. The method can be advantageously used for producing a novel peptide derivative in a com. process. Thus, 20.8 g MeSO3H and 20.0 g tert-Bu chloride were successively added to 10.0 g L-tyrosine Me ester hydrochloride under stirring, stirred at 50° for 5 h, treated dropwise with MeOH (20 mL)/H2O (20 mL) under ice-cooling then with a solution of 14.2 g KOH in 43 mL H2O at <10° to give 77.0% 3-tert-butyl-L-tyrosine Me ester which (8.35 g) was added to a mixture of 24.1 g 62% aqueous ethylamine and 7.52 g ethylamine hydrochloride under ice-cooling and stirred at room temperature for 5 h to give 89.8% 3-tert-butyl-L-tyrosine ethylamide (VI). To a solution of 5.50 g VI and 3.35 g 1-hydroxybenzotriazole monohydrate in 55 mL THF were

successively added 4.19 g 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and 3.04 mL Et3N and stirred at room temperature for 2.5 h to give 100% N-tert-butoxycarbonyl-N-methyl-L-valyl-3-tert-butyl-L-tyrosine ethylamide which (10.0 g) was dissolved in 100 mL EtOAc, treated with 11.1 mL concentrated H2SO4 under ice-cooling, treated with 100 mL EtOAc, adjusted pH 8 by adding saturated aqueous NaHCO3, and stirred 15 min to give 87.9% N-methyl-L-valyl-3-tert-butyl-L-tyrosine ethylamide (VII). To a mixture of 5.50 g VII, 5.20 g N-tert-butoxycarbonyl-N-methyl-4-fluoro-L-phenylalanine, 4.47 g 2-chloro-1-methylpyridinium iodide, and 37 mL tert-Bu Me ether was added 5.09 mL Et3N and stirred at room temperature for 4 h to give 86.0% N-tert-butoxycarbonyl-N-methyl-4-fluoro-L-phenylalanyl-N-methyl-L-valyl-3-tert-butyl-L-tyrosine ethylamide which (7.50 g) was similarly deprotected as described above using concentrated H2SO4 in EtOAc to give 100% N-methyl-4-fluoro-L-phenylalanyl-N-methyl-L-valyl-3-tert-butyl-L-tyrosine.

IT 287210-10-0P 393562-03-3P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation tripeptide derivs. by sequential coupling of N-methyl-L-valine derivs. and L-phenylalanine derivs. to 3-tert-butyl-L-tyrosinamide derivs.)

RN 287210-10-0 HCAPLUS
CN L-Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-4-fluoro-N-methyl-L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)-N-ethyl- (9CI) (CA INDEX NAME)

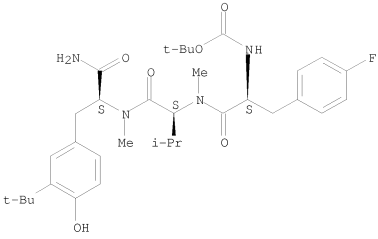
Absolute stereochemistry.



RN 393562-03-3 HCAPLUS
CN L-Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-4-fluoro-L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)-Nα-methyl- (9CI) (CA INDEX NAME)

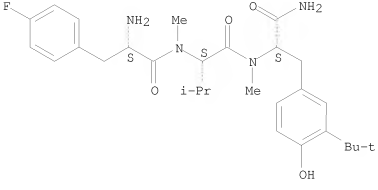
Absolute stereochemistry.

stn



IT 287205-81-6P 287206-61-5P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation tripeptide derivs. by sequential coupling of N-methyl-L-valine derivs. and L-phenylalanine derivs. to 3-tert-butyl-L-tyrosinamide derivs.)
RN 287205-81-6 HCAPLUS
CN L-Tyrosinamide, 4-fluoro-L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)-Nα-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

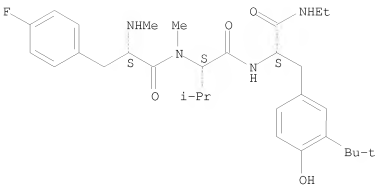


RN 287206-61-5 HCAPLUS
CN L-Tyrosinamide, 4-fluoro-N-methyl-L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)-N-ethyl- (CA INDEX NAME)

Absolute stereochemistry.

Updated Search

stn



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:139868 HCAPLUS
DOCUMENT NUMBER: 130:196958
TITLE: Preparation of 3-tert-butyl-L-tyrosinamide-containing peptides and related compounds exhibiting a motilin receptor antagonism
INVENTOR(S): Kotake, Ken-ichiro; Kozono, Toshiro; Sato, Tsutomu; Takanashi, Hisanori
PATENT ASSIGNEE(S): Chugai Seiyaku Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9909053	A1	19990225	WO 1998-JP3627	19980814
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
TW 460478	B	20011021	TW 1998-87113211	19980811
CA 2301687	A1	19990225	CA 1998-2301687	19980814
AU 9886490	A	19990308	AU 1998-86490	19980814
AU 741216	B2	20011129		
JP 2000044595	A	20000215	JP 1998-229586	19980814
JP 3583928	B2	20041104		
EP 1006122	A1	20000607	EP 1998-937826	19980814
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6255285	B1	20010703	US 2000-485620	20000215
PRIORITY APPLN. INFO.:			JP 1997-255879 A	19970815

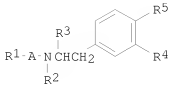
Updated Search

stn

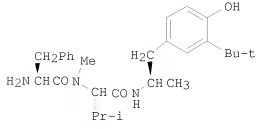
JP 1998-186802 A 19980528
WO 1998-JP3627 W 19980814

OTHER SOURCE(S): MARPAT 130:196958

GI



I



II

AB Phenethylamine derivs. represented by general formula [I; wherein A represents an amino acid or α-substituted amino acid residue; R1 represents R6CO, (un)substituted C2-7 linear or branched alkyl, C3-8 alkenyl, or C3-8 alkynyl; R2 represents hydrogen, C1-3 linear or branched alkyl; R3 represents COR7, (un)substituted C1-5 linear or branched alkyl, C2-5 alkenyl, or C2-5 alkynyl; R4 represents H, C1-6 linear or branched alkyl, C2-6 alkenyl, C2-6 alkynyl, etc.; R5 represents hydroxy or C1-4 n-alkoxy; R6 represents (un)substituted C1-6 linear or branched alkyl, C2-7 alkenyl, or C2-7 alkynyl, optionally benzene- or heterocyclic ring-condensed C3-7 cycloalkyl, (un)substituted C6-12 aromatic ring, (un)substituted C3-12 (un)saturated heterocyclic ring, (un)substituted NH2, (un)substituted linear or branched C1-5 alkoxy, C2-6 alkenyloxy, C2-6 alkynyloxy, etc.; and R7 represents H, (un)substituted C1-5 linear or branched alkyl, C3-7 cycloalkyl, (un)substituted NH2, OH, linear or branched alkyl C1-6 alkoxy, or C3-7 cycloalkyloxy] are prepared Also claimed are a motilin receptor antagonist, an inhibitor of digestive tract motility, and a remedy for high blood motilin. They are also useful for the treatment of irritable bowel syndrome. Thus, Nα-methyl-N-[2-(3-tert-butyl-4-hydroxyphenyl)-1-methylethyl]-L-valinamide was condensed with Boc-Phe-OH using HOBT and DIC in DMF at room temperature for 2.5 days followed by deprotection with CF3CO2H in CH2Cl2 to give the title compound (II). II in vitro showed IC50 of 1.9 nM for inhibiting the binding of [125I]motilin motilin receptor preparation from rabbit ileum mucous membrane.

Updated Search

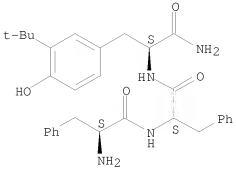
stn

IT 220806-45-1P 220806-47-3P 220806-49-5P
220806-51-9P 220806-59-7P 220806-61-1P
220806-63-3P 220806-71-3P 220806-75-7P
220806-77-9P 220806-79-1P 220806-81-5P
220806-83-7P 220806-85-9P 220806-87-1P
220806-89-3P 220806-91-7P 220806-93-9P
220806-95-1P 220806-97-3P 220806-99-5P
220807-01-2P 220807-03-4P 220807-05-6P
220807-07-8P 220807-09-0P 220807-11-4P
220807-19-2P 220808-16-2P 220808-17-3P
220808-18-4P 220808-19-5P 220808-20-8P
220808-27-5P 220808-28-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-tert-butyl-L-tyrosinamide-containing peptide compds. as motilin receptor antagonists, inhibitors of digestive tract motility, and remedy for high blood motilin)
RN 220806-45-1 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-phenylalanyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-44-0
CMF C31 H38 N4 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

Updated Search

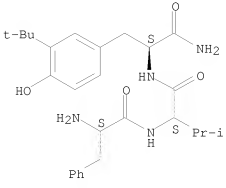
stn

RN 220806-47-3 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-valyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-46-2
CMF C27 H38 N4 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 220806-49-5 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-alanyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

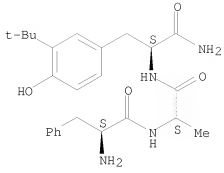
CM 1

CRN 220806-48-4
CMF C25 H34 N4 O4

Absolute stereochemistry.

Updated Search

stn



CM 2

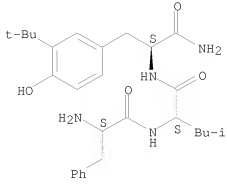
CRN 76-05-1
CMF C2 H F3 O2

RN 220806-51-9 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-leucyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-50-8
CMF C28 H40 N4 O4

Absolute stereochemistry.



CM 2

Updated Search

stn

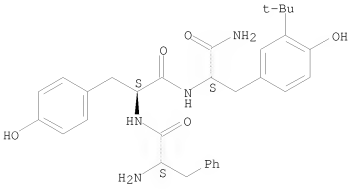
CRN 76-05-1
CMF C2 H F3 O2

RN 220806-59-7 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-tyrosyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-58-6
CMF C31 H38 N4 O5

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 220806-61-1 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-(αS)-α-aminobenzenebutanoyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

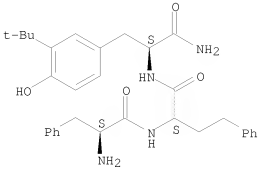
Updated Search

stn

CM 1

CRN 220806-60-0
CMF C32 H40 N4 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 220806-63-3 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-3-(2-thienyl)-L-alanyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

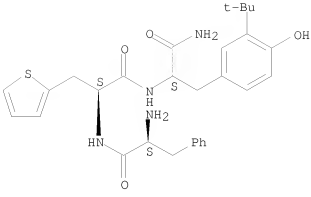
CM 1

CRN 220806-62-2
CMF C29 H36 N4 O4 S

Absolute stereochemistry.

Updated Search

stn



CM 2

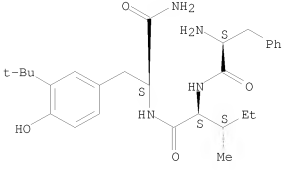
CRN 76-05-1
CMF C2 H F3 O2

RN 220806-71-3 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-isoleucyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-70-2
CMF C28 H40 N4 O4

Absolute stereochemistry.



CM 2

Updated Search

stn

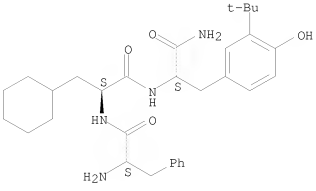
CRN 76-05-1
CMF C2 H F3 O2

RN 220806-75-7 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-3-cyclohexyl-L-alanyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-74-6
CMF C31 H44 N4 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 220806-77-9 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-3-methyl-L-valyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

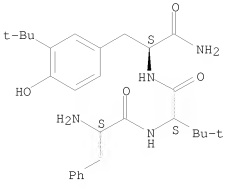
Updated Search

stn

CM 1

CRN 220806-76-8
CMF C28 H40 N4 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 220806-79-1 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-α-asparty1-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

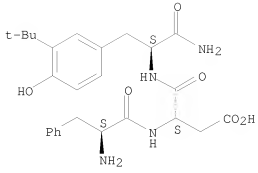
CM 1

CRN 220806-78-0
CMF C26 H34 N4 O6

Absolute stereochemistry.

Updated Search

stn



CM 2

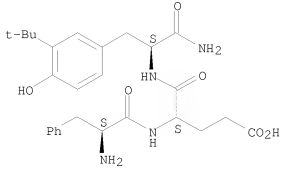
CRN 76-05-1
CMF C2 H F3 O2

RN 220806-81-5 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-α-glutamyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-80-4
CMF C27 H36 N4 O6

Absolute stereochemistry.



CM 2

Updated Search

stn

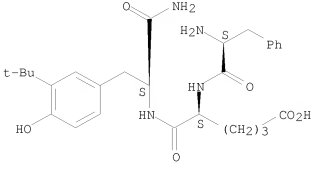
CRN 76-05-1
CMF C2 H F3 O2

RN 220806-83-7 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-5-carboxy-L-norvalyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-82-6
CMF C28 H38 N4 O6

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 220806-85-9 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-asparaginyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

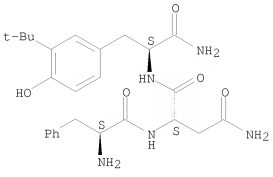
CM 1

Updated Search

stn

CRN 220806-84-8
CMF C26 H35 N5 O5

Absolute stereochemistry.



CM 2

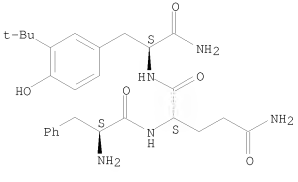
CRN 76-05-1
CMF C2 H F3 O2

RN 220806-87-1 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-glutaminyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-86-0
CMF C27 H37 N5 O5

Absolute stereochemistry.



Updated Search

stn

CM 2

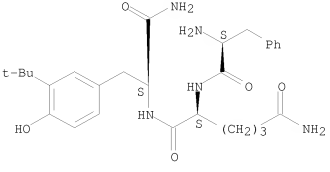
CRN 76-05-1
CMF C2 H F3 O2

RN 220806-89-3 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-6-oxo-L-lysyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-88-2
CMF C28 H39 N5 O5

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 220806-91-7 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-(2S)-2,4-diaminobutanoyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

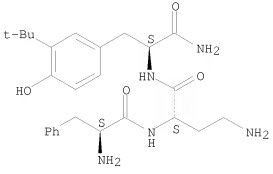
Updated Search

stn

CM 1

CRN 220806-90-6
CMF C26 H37 N5 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 220806-93-9 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-ornithyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

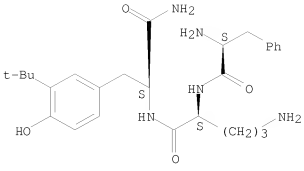
CM 1

CRN 220806-92-8
CMF C27 H39 N5 O4

Absolute stereochemistry.

Updated Search

stn



CM 2

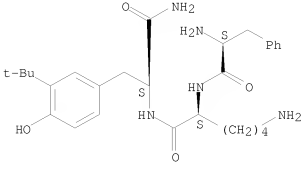
CRN 76-05-1
CMF C2 H F3 O2

RN 220806-95-1 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-lysyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-94-0
CMF C28 H41 N5 O4

Absolute stereochemistry.



CM 2

Updated Search

stn

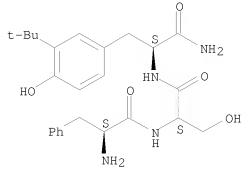
CRN 76-05-1
CMF C2 H F3 O2

RN 220806-97-3 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-seryl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-96-2
CMF C25 H34 N4 O5

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 220806-99-5 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-homoseryl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

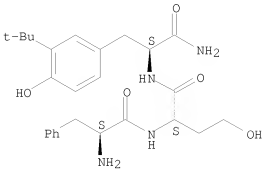
CM 1

Updated Search

stn

CRN 220806-98-4
CMF C26 H36 N4 O5

Absolute stereochemistry.



CM 2

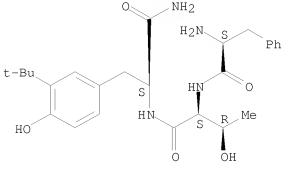
CRN 76-05-1
CMF C2 H F3 O2

RN 220807-01-2 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-threonyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220807-00-1
CMF C26 H36 N4 O5

Absolute stereochemistry.



Updated Search

stn

CM 2

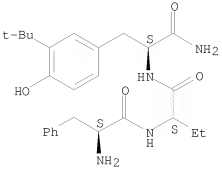
CRN 76-05-1
CMF C2 H F3 O2

RN 220807-03-4 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-(2S)-2-aminobutanoyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220807-02-3
CMF C26 H36 N4 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 220807-05-6 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-norvalyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

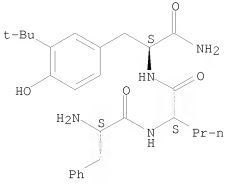
Updated Search

stn

CM 1

CRN 220807-04-5
CMF C27 H38 N4 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 220807-07-8 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-methionyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

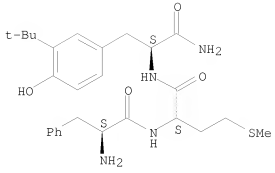
CM 1

CRN 220807-06-7
CMF C27 H38 N4 O4 S

Absolute stereochemistry.

Updated Search

stn



CM 2

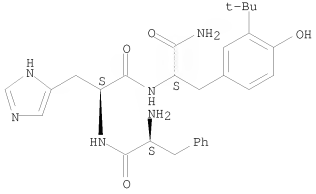
CRN 76-05-1
CMF C2 H F3 O2

RN 220807-09-0 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-histidyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220807-08-9
CMF C28 H36 N6 O4

Absolute stereochemistry.



CM 2

Updated Search

stn

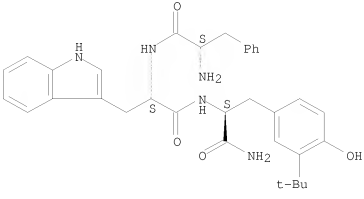
CRN 76-05-1
CMF C2 H F3 O2

RN 220807-11-4 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-tryptophyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220807-10-3
CMF C33 H39 N5 O4

Absolute stereochemistry.



CM 2

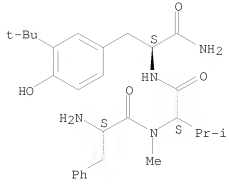
CRN 76-05-1
CMF C2 H F3 O2

RN 220807-19-2 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Updated Search

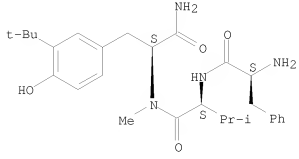
stn

Absolute stereochemistry.



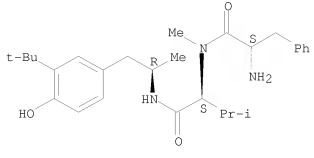
RN 220808-16-2 HCAPLUS
CN L-Tyrosinamide, L-phenylalanyl-L-valyl-3-(1,1-dimethylethyl)-Nα-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220808-17-3 HCAPLUS
CN L-Valinamide, L-phenylalanyl-N-[(1R)-2-[3-(1,1-dimethylethyl)-4-hydroxyphenyl]-1-methylethyl]-N2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



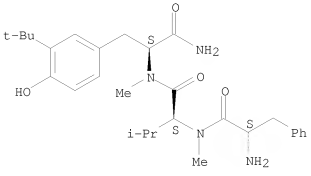
RN 220808-18-4 HCAPLUS

Updated Search

stn

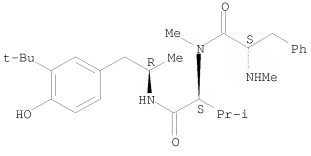
CN L-Tyrosinamide, L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)-Nα-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



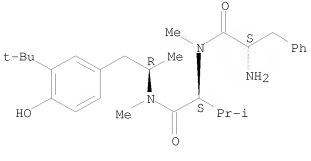
RN 220808-19-5 HCAPLUS
CN L-Valinamide, N-methyl-L-phenylalanyl-N-[(1R)-2-[3-(1,1-dimethylethyl)-4-hydroxyphenyl]-1-methylethyl]-N2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220808-20-8 HCAPLUS
CN L-Valinamide, L-phenylalanyl-N-[(1R)-2-[3-(1,1-dimethylethyl)-4-hydroxyphenyl]-1-methylethyl]-N,N2-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

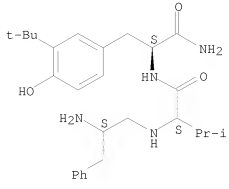


Updated Search

stn

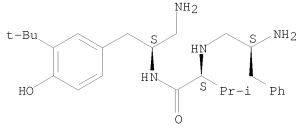
RN 220808-27-5 HCAPLUS
CN L-Tyrosinamide, N-[(2S)-2-amino-3-phenylpropyl]-L-valyl-3-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220808-28-6 HCAPLUS
CN Butanamide, N-[(1S)-2-amino-1-[[3-(1,1-dimethylethyl)-4-hydroxyphenyl]methyl]ethyl]-2-[[(2S)-2-amino-3-phenylpropyl]amino]-3-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

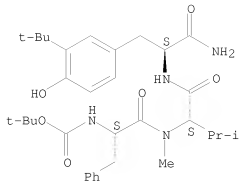


IT 220808-36-6P 220808-44-6P 220808-74-2P
220808-80-0P 220808-85-5P 220808-89-9P
220808-90-2P 220808-96-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3-tert-butyl-L-tyrosinamide-containing peptide compds. as motilin receptor antagonists, inhibitors of digestive tract motility, and remedy for high blood motilin)
RN 220808-36-6 HCAPLUS
CN L-Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

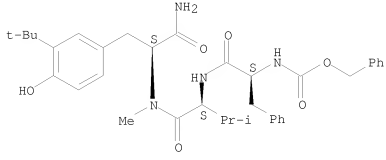
Updated Search

stn



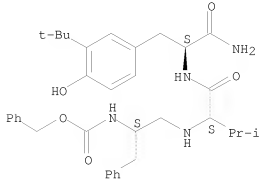
RN 220808-44-6 HCAPLUS
CN L-Tyrosinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-L-valyl-3-(1,1-dimethylethyl)-Nα-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220808-74-2 HCAPLUS
CN L-Tyrosinamide, N-[(2S)-3-phenyl-2-[[(phenylmethoxy)carbonyl]amino]propyl]-L-valyl-3-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



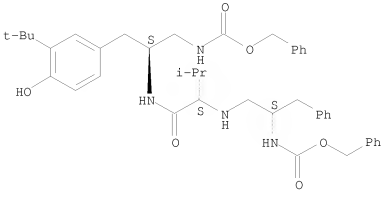
RN 220808-80-0 HCAPLUS

Updated Search

stn

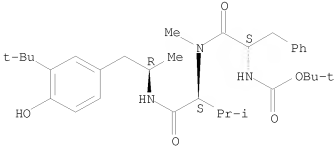
CN 2,5,8,11-Tetraazadodecanedioic acid, 9-[[3-(1,1-dimethylethyl)-4-hydroxyphenyl]methyl]-6-(1-methylethyl)-7-oxo-3-(phenylmethyl)-, 1,12-bis(phenylmethyl) ester, (3S,6S,9S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 220808-85-5 HCAPLUS
CN L-Valinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[(1R)-2-[3-(1,1-dimethylethyl)-4-hydroxyphenyl]-1-methylethyl]-N2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

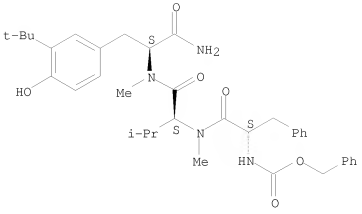


RN 220808-89-9 HCAPLUS
CN L-Tyrosinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)-Nα-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

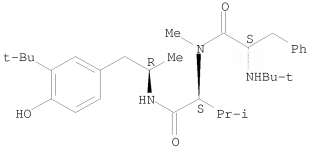
Updated Search

stn



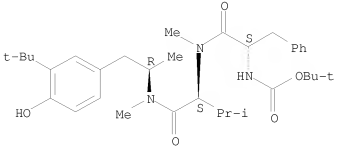
RN 220808-90-2 HCAPLUS
CN L-Valinamide, N-(1,1-dimethylethyl)-L-phenylalanyl-N-[(1R)-2-[3-(1,1-dimethylethyl)-4-hydroxyphenyl]-1-methylethyl]-N2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220808-96-8 HCAPLUS
CN L-Valinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[(1R)-2-[3-(1,1-dimethylethyl)-4-hydroxyphenyl]-1-methylethyl]-N,N2-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Updated Search

stn

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 16:30:09 ON 26 OCT 2008)

FILE 'REGISTRY' ENTERED AT 16:30:25 ON 26 OCT 2008
L1 STRUCTURE UPLOADED
L2 4 S L1
L3 80 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 16:39:11 ON 26 OCT 2008
L4 29 S L3
L5 1 S LL AND MATSUOKA, H?/AU
L6 29 S L4 NOT L5
L7 29 S L4 NOT L5
L8 0 S L4 AND SATO, T?/AU
L9 0 S L6 AND TAKAHASHI, T?/AU

FILE 'REGISTRY' ENTERED AT 16:42:14 ON 26 OCT 2008
L10 STRUCTURE UPLOADED
L11 4 S L10
L12 414 S L10 FULL

FILE 'HCAPLUS' ENTERED AT 16:45:11 ON 26 OCT 2008
L13 8 S L12
L14 2 S L13 AND MATSUOKA, H?/AU
L15 6 S L13 NOT L14
L16 2 S L15 AND SATO, T?/AU

=> s l15 not l16
L17 4 L15 NOT L16

=> s l17 and takahashi, t?/au
21947 TAKAHASHI, T?/AU
L18 0 L17 AND TAKAHASHI, T?/AU

=> s l17 and kim, d?/au
31091 KIM, D?/AU
L19 1 L17 AND KIM, D?/AU

=> d l19, ibib abs hitstr, 1

L19 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:637704 HCAPLUS
DOCUMENT NUMBER: 137:185838
TITLE: Process for preparation of peptide derivatives
INVENTOR(S): Kim, Dong Ick; Jeon, Gee Ho; Kim, Sung Jin
PATENT ASSIGNEE(S): Chugai Seiyaku Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1

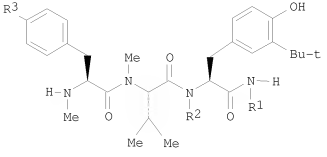
Updated Search

stn

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064623	A1	20020822	WO 2002-JP1139	20020212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002230216	A1	20020828	AU 2002-230216	20020212
PRIORITY APPLN. INFO.:			KR 2001-6673	A 20010212
			WO 2002-JP1139	W 20020212

OTHER SOURCE(S): CASREACT 137:185838; MARPAT 137:185838
GI



I

AB The title compds. I [R1 is hydrogen or linear or branched C1-4 alkyl; R2 is hydrogen or linear or branched C1-4 alkyl; and R3 is halogeno] are prepared in a multistep process. I are motilin receptor antagonists and are useful as drugs for gastric or intestinal diseases (no data). Thus, amidation of N-(tert-butoxycarbonyl)-L-(4-fluorophenyl)alanine with L-valine Me ester hydrochloride, followed by methylation with iodomethane, saponification, reaction with 3-tert-butyl-L-tyrosine Et amide, and deprotection, gave N-methyl-L-4-fluorophenylalanyl-N-methyl-L-valine-3-tert-butyl-L-tyrosine Et amide.

IT 287206-61-5P
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for preparation of peptide derivs.)

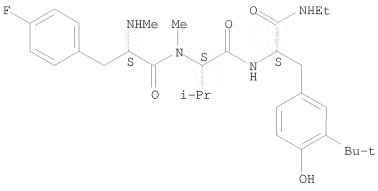
RN 287206-61-5 HCAPLUS

CN L-Tyrosinamide, 4-fluoro-N-methyl-L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)-N-ethyl- (CA INDEX NAME)

Updated Search

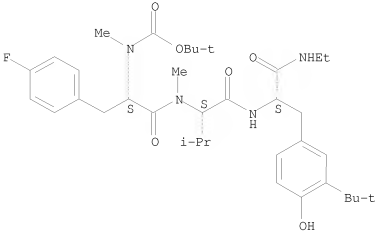
stn

Absolute stereochemistry.



IT 287210-10-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of peptide derivs.)
RN 287210-10-0 HCAPLUS
CN L-Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-4-fluoro-N-methyl-L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)-N-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 16:30:09 ON 26 OCT 2008)

FILE 'REGISTRY' ENTERED AT 16:30:25 ON 26 OCT 2008
L1 STRUCTURE UPLOADED

Updated Search

stn

```
L2            4 S L1
L3           80 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 16:39:11 ON 26 OCT 2008
L4           29 S L3
L5            1 S LL AND MATSUOKA, H?/AU
L6           29 S L4 NOT L5
L7           29 S L4 NOT L5
L8            0 S L4 AND SATO, T?/AU
L9            0 S L6 AND TAKAHASHI, T?/AU

     FILE 'REGISTRY' ENTERED AT 16:42:14 ON 26 OCT 2008
L10             STRUCTURE UPLOADED
L11           4 S L10
L12         414 S L10 FULL

     FILE 'HCAPLUS' ENTERED AT 16:45:11 ON 26 OCT 2008
L13           8 S L12
L14           2 S L13 AND MATSUOKA, H?/AU
L15           6 S L13 NOT L14
L16           2 S L15 AND SATO, T?/AU
L17           4 S L15 NOT L16
L18           0 S L17 AND TAKAHASHI, T?/AU
L19           1 S L17 AND KIM, D?/AU

=> s l17 not l19
L20           3 L17 NOT L19

=> s l20 and jung, k?/au
          3311 JUNG, K?/AU
L21           0 L20 AND JUNG, K?/AU

=> s l20 and park, c?/au
         12728 PARK, C?/AU
L22           0 L20 AND PARK, C?/AU

=> d l20, ibib abs fhitstr, 1-3

L20  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2008:172923  HCAPLUS
DOCUMENT NUMBER:          148:299702
TITLE:                    Oral administration of MA-2029, a novel selective and
                          competitive motilin receptor antagonist, inhibits
                          motilin-induced intestinal contractions and visceral
                          pain in rabbits
AUTHOR(S):                Sudo, Hirokazu; Yoshida, Shoshin; Ozaki, Ken-ichi;
                          Muramatsu, Hiroyasu; Onoma, Mitsu; Yogo, Kenji; Kamei,
                          Kenshi; Cynshi, Osamu; Kuromaru, Osamu; Peeters, Theo
                          L.; Takanashi, Hisanori
CORPORATE SOURCE:         Fuji-Gotemba Research Laboratories, Chugai
                          Pharmaceutical Co., Ltd., Shizuoka, 412-8513, Japan
SOURCE:                   European Journal of Pharmacology (2008), 581(3),
                          296-305
                          CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER:                Elsevier B.V.
DOCUMENT TYPE:            Journal
```

Updated Search

LANGUAGE: English

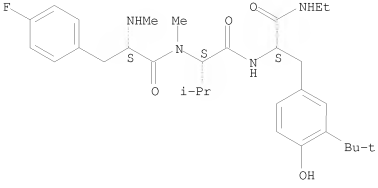
AB The pharmacol. properties of MA-2029, a novel motilin receptor antagonist, were investigated. In vitro, MA-2029 (1 to 30 nM) competitively inhibited motilin-induced contractions in isolated rabbit duodenal longitudinal muscle strips, with a pA2 value of 9.17 ± 0.01 (n = 5). However, contractile responses to acetylcholine and substance P were unaffected even at 1 μM of MA-2029. MA-2029 concentration-dependently inhibited the binding of [125I]motilin to motilin receptors in a homogenate of rabbit colon smooth muscle tissue and membranes of HEK 293 cells expressing human motilin receptors. The pKi of MA-2029 was 8.58 ± 0.04 in the rabbit colon homogenate (n = 4) and 8.39 in the HEK 293 cells (mean of duplicate expts.). In vivo, orally-administered MA-2029 (3 to 30 mg/kg) dose-dependently inhibited colonic contractions induced by motilin (3 μg/kg, i.v.) in conscious rabbits. Inhibition was caused by all doses at 30 min after administration and by 10 mg/kg or more at 4 h after administration. The plasma concentration of MA-2029 correlated with its inhibitory effect. Furthermore, the oral administration of MA-2029 (0.3 to 3 mg/kg) also inhibited abdominal muscle contractions (an index of the visceral pain) induced by i.v. infusion of motilin (3 μg/kg/h) during colorectal distension in conscious rabbits. These results indicate that MA-2029 is an orally active, selective and competitive motilin receptor antagonist. It is suggested that this compound may be useful for gastrointestinal disorders associated with disturbed gastrointestinal motility such as irritable bowel syndrome.

IT 287206-61-5, MA-2029
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral motilin receptor antagonist MA-2029 inhibits intestinal contractions and visceral pain)

RN 287206-61-5 HCAPLUS

CN L-Tyrosinamide, 4-fluoro-N-methyl-L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)-N-ethyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:106928 HCAPLUS
DOCUMENT NUMBER: 148:221501

stn

TITLE: Characterization of MA-2029 hydrochloride solvates, desolvates, and a hydrate
AUTHOR(S): Takata, Noriyuki; Hayashi, Yoshiki; Machida, Minoru; Terada, Katsuhide
CORPORATE SOURCE: Department of Pharmaceutics, Faculty of Pharmaceutical Science, Toho University, 2-2-1 Miyama, Funabashi, Chiba, 274-8501, Japan
SOURCE: Asian Journal of Pharmaceutical Sciences (Hong Kong, China) (2006), 1(3-4), 146-158
CODEN: AJPSGU; ISSN: 1818-0876
PUBLISHER: Hong Kong Asiamed Publish House
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: To characterize the desolvation and hydration behavior of MA-2029 hydrochloride solvates, desolvates, and a hydrate. Methods: MA-2029 hydrochloride solvates, desolvates, and a hydrate were characterized by powder X-ray diffraction, crystal structure determination, moisture sorption anal., and differential scanning calorimetry. Results: The solvates crystallized from acetonitrile/water and Et acetate saturated with water were identified as acetonitrile solvated hemihydrate and Et acetate solvated hemihydrate, resp. Both solvates possessed essentially similar lattice parameters and similar MA-2029 conformations despite having different solvents, and had tunnel structures filled with the solvent mols., which were maintained after desolvation. After desolvation, the vacant tunnels caused nonstoichiometric and extreme hygroscopicity at low relative humidity and they were maintained upon hydration. On heating the hydrate, disruption of the crystal lattice after dehydration was observed prior to melting and this was reflected in the enthalpies of fusion of the dehydrate that fell as the heating rate was reduced. Conclusions: MA-2029 hydrochloride solvates were classified as clathrates which possess tunnel structures. The tunnel structures caused their several specific physicochem. features in the desolvation and hydration processes: isomorphism between both solvates despite having different solvents, hydration into vacant tunnels created after desolvation, and disruption of crystal lattices of the dehydrate prior to melting during the heating process.

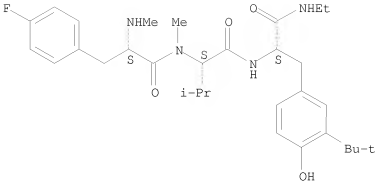
IT 922190-03-2, MA 2029 hydrochloride
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MA-2029 hydrochloride solvates like acetonitrile solvated hemihydrate and Et acetate solvated hemihydrate showed similar lattice parameters and had tunnel structures filled with solvent, which were maintained after desolvation)

RN 922190-03-2 HCAPLUS
CN L-Tyrosinamide, 4-fluoro-N-methyl-L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)-N-ethyl-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.

Updated Search

stn



● HCl

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1298385 HCAPLUS
DOCUMENT NUMBER: 146:177451
TITLE: Delineation of the motilin domain involved in desensitization and internalization of the motilin receptor by using full and partial antagonists
AUTHOR(S): Mitselos, Anna; Depoortere, Inge; Peeters, Theo L.
CORPORATE SOURCE: Centre for Gastroenterological Research, Catholic University of Leuven, Louvain, B-3000, Belg.
SOURCE: Biochemical Pharmacology (2007), 73(1), 115-124
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Studies with fragments of the gastrointestinal peptide, motilin, indicate that the C-terminal region of this peptide plays an important role in the desensitization of the motilin receptor (MTLR). To verify this hypothesis, we studied the desensitization, phosphorylation and internalization induced by motilin analogs of different chain length with agonistic and antagonistic properties in CHO-MTLR cells. We studied motilin [1-22], the [1-14] fragment, the analogs Phe3[1-22] and Phe3[1-14], and two putative antagonists, GM-109 and MA-2029 (modified 1-4 and 1-3 fragments). Activation and desensitization (2 h preincubation with the motilin analogs 10 μM) were studied in CHO-MTLR cells by an aequorin based luminescence assay. Phosphorylation was studied by immunopptn. and internalization was visualized in CHO-MTLR cells containing an enhanced green fluorescent protein (CHO-MTLR-EGFP). Results showed that Motilin [1-22] and [1-14] were more potent than Phe3[1-22] and Phe3[1-14] (pEC50: 9.77, 8.78, 7.36 and 6.65, resp.) to induce Ca2+ release. GM-109 and MA-2029 were without agonist activity. Motilin[1-22] and Phe3[1-22] decreased the second response to motilin from 78±2% to 11±3% and 34±3% ($P < 0.001$), resp., whereas [1-14], Phe3[1-14], GM-109 and MA-2029 had no desensitizing effect (68±5%, 78±3%, 78±6% and 78±5%, resp., $P > 0.05$). The rank order of MTLR-phosphorylation was:

stn

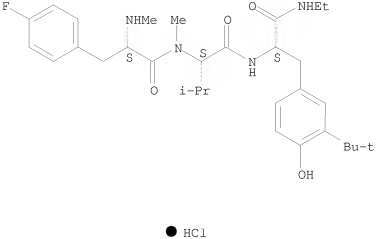
[1-22] > [1-14] > Phe3[1-22] = Phe3[1-14] > GM-109 = MA-2029. Only motilin [1-22] and [1-14] induced receptor MTLR-EGFP internalization as shown by a decrease in membrane fluorescence: 20±3% and 7±3%, resp. Thus, the C-terminus of motilin enhances desensitization, phosphorylation and internalization of the MTLR while modifications of the N-terminus can favor a conformation of the receptor that is less susceptible to phosphorylation and internalization.

IT 922190-03-2, MA 2029
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); PRP (Properties); BIOL (Biological study)
(motilin receptor antagonist; delineation of motilin domain involved in desensitization, phosphorylation and internalization of motilin receptor by using full and partial antagonists)

RN 922190-03-2 HCAPLUS

CN L-Tyrosinamide, 4-fluoro-N-methyl-L-phenylalanyl-N-methyl-L-valyl-3-(1,1-dimethylethyl)-N-ethyl-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file caold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	73.19	457.30
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-6.40	-7.20

FILE 'CAOLD' ENTERED AT 16:51:42 ON 26 OCT 2008

Updated Search

```
stn


FILE COVERS 1907-1966
FILE LAST UPDATED:  01 May 1997 (19970501/UP)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.  Title keywords, authors, patent
  assignees, and patent information, e.g., patent numbers, are
  now searchable from 1907-1966.  TIFF images of CA abstracts
  printed between 1907-1966 are available in the PAGE
  display formats.

  New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file supports REGlstRY for direct browsing and searching of
  all substance data from the REGISTRY file.  Enter HELP FIRST for
  more information.

  CAOLD will be discontinued and removed from associated database
  clusters.

    . November 22, 2008 - removed from database clusters
    . December 31, 2008 - removed from STN

  Content previously available only in CAOLD is now available
  in CA/CAplus.  To learn more about the options available for
  transferring saved search queries and answer sets to CA/CAplus,
  contact your STN Service Center.

=> d his

     (FILE 'HOME' ENTERED AT 16:30:09 ON 26 OCT 2008)

     FILE 'REGISTRY' ENTERED AT 16:30:25 ON 26 OCT 2008
L1               STRUCTURE UPLOADED
L2             4 S L1
L3            80 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 16:39:11 ON 26 OCT 2008
L4            29 S L3
L5             1 S LL AND MATSUOKA, H?/AU
L6            29 S L4 NOT L5
L7            29 S L4 NOT L5
L8             0 S L4 AND SATO, T?/AU
L9             0 S L6 AND TAKAHASHI, T?/AU

     FILE 'REGISTRY' ENTERED AT 16:42:14 ON 26 OCT 2008
L10              STRUCTURE UPLOADED
L11            4 S L10
L12          414 S L10 FULL

     FILE 'HCAPLUS' ENTERED AT 16:45:11 ON 26 OCT 2008
L13            8 S L12
L14            2 S L13 AND MATSUOKA, H?/AU
L15            6 S L13 NOT L14
L16            2 S L15 AND SATO, T?/AU
L17            4 S L15 NOT L16
L18            0 S L17 AND TAKAHASHI, T?/AU



Updated Search
```

stn

```
L19             1 S L17 AND KIM, D?/AU
L20             3 S L17 NOT L19
L21             0 S L20 AND JUNG, K?/AU
L22             0 S L20 AND PARK, C?/AU

     FILE 'CAOLD' ENTERED AT 16:51:42 ON 26 OCT 2008

=> s l12
L23           0 L12
```

Updated Search